## REMARKS

Claims 33-82 are pending in the present application, and claims 41-53, 63-72, and 79-82 are withdrawn from consideration. Reconsideration and allowance of the claims is respectfully requested in view of the following remarks.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 33-40, 54-61, and 73-78 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

The pending claims are directed to an antisense oligonucleotide, wherein the antisense oligonucleotide inhibits the expression of a nucleic acid molecule encoding a human EDG-1 or EDG-3 receptor and wherein the antisense oligonucleotide includes the translational initiation site of the nucleic acid molecule encoding the human EDG-1 or EDG-3 receptor. Applicants note that as they present claims are specifically directed to an antisense oligonucleotide including the translational initiation site of the nucleic acid molecule encoding the human EDG-1 or EDG-3 receptor.

In making the rejection, the Examiner states "Applicants suggest[] that with the knowledge of the EDG-1 and EDG-3 sequences one could readily make antisense targeting these sequences, however it is apparent that Applicant is suggesting that further experimentation be performed in order to isolate the claimed invention". (12/19/2003 Office Action, pages 2-3) Applicants strongly disagree with the Examiner.

As illustrated in the present Application, Applicants have reduced to practice two antisense oligonucleotides to human EDG-1 (SEQ ID NOs. 1 and 2) and one antisense oligonucleotide to EDG-3 (SEQ ID NO. 5). In these cases, the antisense oligonucleotides include the translation initiation site. As stated in a previous Amendment, the NIH Medical Subject Headings define an oligonucleotide as polymer made up of a few (2-20)

nucleotides. Given the definition of oligonucleotide and the requirement that the oligonucleotide include the translation initiation codon, one of ordinary skill in the art could readily design an oligonucleotide that meets these criteria based on the nucleotide sequences for human EDG-1 and EDG-3 which have been entered by sequence amendment.

Enablement is not precluded even if some experimentation is necessary, provided the amount is not unduly excessive, *Bruning v. Hirose* (CAFC 1998) 161 F.3d 861, 48PQ2d 1934, citing *Hybritech, Inc. v. Monoclonal Antibodies Inc.* (CAFC 1986) 802 F.2d 1367, 231 USPQ 81.

Applicants submit that based on the description in the Specification, making and testing antisense oligonucleotides that include the initiation codon of human EDG-1 or EDG-3 does not require undue experimentation. The sequences of human EDG-1 and EDG-3 are provided, and making antisense oligonucleotides corresponding to these sequences is routine. Further, Applicants have identified the region including the initiation codon as accessible to antisense oligonucleotides. Thus, only routine experimentation is required to produce additional antisense oligonucleotides as presently claimed.

The Examiner then goes on to state "The claims are broadly drawn to an undefined genus of nucleic acid sequences, which might hybridize to an undefined genus of nucleic acid sequences, which might hybridize to an undefined genus of target EDG-1, or EDG-3 target genes". (12/19/2003 Office Action, page 3) Applicants again strongly disagree.

The claims are directed to antisense oligonucleotides (i.e., polynucleotides of length 2 to 20) that include the initiation codon. Further, the claims require that the antisense oligonucleotides target human EDG-1 or human EDG-3. Three such oligonucleotides have been reduced to practice. Applicants thus believe that the breadth of the claims is well within the scope of what is described in the application.

The Examiner further states:

> the specification as filed does not teach by way of sequence target EDG-1 or EDG-3 gene[s] from other whole organisms, accessible regions from such sequences for design of antisense, nor specific sequence structure of nucleic acid sequences which function as antisense and have the capability to bind and specifically inhibit a particular target EDG-1 or EDG-3 sequence.

(12/19/2003 Office Action, page 3)

Again, Applicants disagree. First, the claims are directed to antisense oligonucleotides to human EDG-1 or EDG-3, not "other whole organisms" as alleged by the Examiner. Second, the translation initiation codon of human EDG-1 and human EDG-3 have been by example shown to be accessible to antisense inhibition (See, Example 12, pp. 35-37 of the Application as filed). The claims are not directed to all sequence regions, but a sequence region that has been shown to be accessible to antisense oligonucleotides. Third, the sequence structure of the human EDG-1 and EDG-3 genes is now included in the application as the Examiner has entered Applicants amended nucleotide sequence listing into the application because it is "technically sound". Finally, SEQ ID NOs. 1, 2 and 5 demonstrate, by way of example, antisense oligonucleotides that include the translation initiation codon and that inhibit human EDG-1 or human EDG-3 gene expression. Thus, all of the concerns raised by the Examiner have been addressed and resolved previously.

In summary, the Examiner states:

> a mere wish or plan to identify antisense oligonucleotides that function to bind and inhibit expression of EDG-1 or EDG-3 is not sufficient to establish that Applicant's invention was sufficiently reduced to practice such that Applicant's had full possession of the claimed invention at the time of filing of the instant invention.

(12/19/2003 Office Action, page 3)

Applicants submit that they were in possession of the invention as it is currently claimed at the time of filing. Three antisense oligonucleotides that include the translation initiation codon and that inhibit human EDG-1 or human EDG-3 gene expression were

reduced to practice in the application as filed. The data in the application clearly shows that these oligonucleotides inhibit expression of the human EDG gene to which they are directed. Based on the Applicants disclosure, only routine experimentation is required to produce antisense oligonucleotides with the scope of the Applicants' claims. Applicants believe that all of the concerns pointed out by the Examiner in this Office Action have been addressed previously by Applicants and clearly overcome by the previous amendments to the claims.

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and allowance is requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130 maintained by Cantor Colburn LLP.

Respectfully submitted,

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